4/3,K/22 (Item 1 from file: 156)
DIALOG(R)File 156:Toxline(R)

02537123 Subfile: TOXBIB-92-113079
Hair growth effects of oral administration of finasteride, a steroid 5 alpha-reductase inhibitor, alone and in combination with topical minoxidil in the balding stumptail macaque.
Diani AR; Mulholland MJ; Shull KL; Kubicek MF; Johnson GA; Schostarez HJ; Brunden MN; Buhl AE
Upjohn Laboratories, Kalamazoo, Michigan 49001.
Source: J Clin Endocrinol Metab; VOL 74, ISS 2, 1992, P345-50 ISSN: 0021-972X Coden: HRB
Language: ENGLISH
Document Type: JOURNAL ARTICLE

Hair growth effects of oral administration of finasteride, a steroid 5 alpha-reductase inhibitor, alone and...
Diani AR; Mulholland MJ; Shull KL; Kubicek MF; Johnson GA; Schostarez HJ; Brunden MN; Buhl AE
... in combination with topical 2% minoxidil, for 20 weeks to determine the effects on scalp **hair** growth in balding adult male stumptail macaque monkeys. A 7-day dose-finding study showed...

... doses of the drug produced a similar diminution in serum dihydrotestosterone (DHT) in male stumptails. **Hair** growth was evaluated by shaving and weighing scalp **hair** at baseline and at 4-week intervals during treatment to obtain cumulative delta **hair** weight (sum of the 4-week changes in **hair** weight from baseline) for the 20-week study. The activity of the 5 alpha-reductasé...

... DHT at 4-week intervals. The combination of finasteride and minoxidil generated significant augmentation of **hair** weight (additive effect) compared to either drug alone. Finasteride increased **hair** weight in four of five monkeys. When the data of the one nonresponsive monkey were excluded, finasteride elicited a significant elevation in **hair** weight compared to topical vehicle alone. Minoxidil also evoked a significant increase in **hair** weight compared to vehicle alone. Serum T was unchanged, whereas serum DHT was significantly depressed...
... T to DHT by this 5 alpha-reductase inhibitor reverses the balding process and enhances **hair** regrowth by topical minoxidil in the male balding stumptail macaque.
Descriptors/Keywords: Androstenes--Pharmacology--PD; *Azasteroids --Pharmacology--PD; *Hair--Drug Effects--DE; *Minoxidil--Pharmacology --PD; *Testosterone 5-alpha-Reductase--Antagonists and Inhibitors--AI...; Administration and Dosage--AD; Azasteroids--Administration and Dosage--AD; Chromatography, High Pressure Liquid; Drug Interactions; **Hair** --Physiology--PH; Macaca; Minoxidil--Administration and Dosage--AD; Minoxidil--Urine--UR; Reference Values; Stanolone--Blood...

L5 ANSWER 7 OF 13 USPATFULL

SUMM . . . and 5%; vegetal proteolytic enzimes, specially papain between 0.1 and 2%, bromelain, between 0.1 and 0.5%; antialopecia products, such as **progesterone** (between 1 and 3%) **minoxidil** (from 1-3%), tricopeptides (0.01-2%) and tricosacarides (0.1-2%), **hair** decolorants, specially mandarin essential oil (0.5-5%) and other **hair** growth retarding substances, such as alkyl-isoquinoleine bromide (0.2-3%).

SUMM . . . and 5%; vegetal proteolytic enzymes, specially papain between 0.1 and 2%, bromclain, between 0.1 and 0.5%; antialopecia products, such as **progesterone** (between 1 and 3%), **minoxidil** (from 1-3%), tricopeptides (0.01-2%) and tricosacarides (0.1-2%, **hair** decolorants, specially mandarin essential oil (0.5-5%) and basic hydroquinone (1-3%); topical use antibiotics, specially basic erythromicin (1-3%), and clindamicin (0.5-1%);. . . and the association with other chemical antiandrogens (cyproterone acetate. Flutemide and Finastiride. Casodex, etc. between 0.01 and 2%) and other **hair** growth retarding substances, such as alkyl-soquinoleine bromide (0.2-5%).

PI US 6113926 20000905

L5 ANSWER 6 OF 13 USPATFULL

CLM What is claimed is:

8. The method of claim 7 which additionally comprises a second **hair** growth agent selected from the group consisting of zinc salts of carboxylic acids, saponins, other triterpenes such as oleanolic acid and ursolic acid, crataegolic acid, celastrol, asiatic acid, inhibitors of 5-.alpha.-reductase such as **progesterone**, 1,4-methyl-4-azasteroids, in particular 17-.beta.-N,N-diethylcarbamoyl-4-methyl-4-aza-5-.alpha.-androstan-3-one, androgen receptor antagonists such as cyproterone acetate, **Minoxidil**.RTM., azelaic acid and its derivatives, cyclosporin, triiodothyronine, diazoxide, potassium channel openers such as cromakalin, phenytoin and mixtures thereof.

PI US 6124362 20000926

L12 ANSWER 23 OF 25 USPATFULL
DETD . . . enhancers of this invention. Scalp conditions such as alopecia arcata may be treated more effectively by applying agents such as **minoxidil** in **combination** with one of the enhancers of this invention directly to the scalp.
DETD Transdermal patches containing **progesterone** with the following composition are prepared.
DETD 9.2 g of PDMS-382 (Dow Corning) pre-polymer, 300 mg of **progesterone** and 500 mg of 5-Amino-5-ethyl-2-(3-heptyl)-1,3-dioxane are mixed. One drop of polymerization initiator is added and the contents are thoroughly mixed.. . .
CLM What is claimed is:
. . . selected from the group consisting of estradiol, ethinyl estradiol and 1,25-dihydroxy-7-dehydrocholesterol; an antifertility agent selected from the group consisting of **progesterone** and medroxyprogesterone; an antiasthmatic agent selected from the group consisting of theophylline, albuterol and metaproterenol; an antineoplastic and antiviral agent. . .
. . . selected from the group consisting of estradiol, ethinyl estradiol and 1,25-dihydroxy-7-dehydrocholesterol; an antifertility agent selected from the group consisting of **progesterone** and medroxyprogesterone; an antiasthmatic agent selected from the group consisting of theophylline, albuterol and metaproterenol; an antineoplastic and antiviral agent. . .
AN 96:3758 USPATFULL
PI US 5482965 19960109

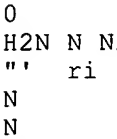
xidil .

The active agents can be administered in a single topical dosage formulation, or each active agent can be administered in. . . dosage formulation, e.g., in separate topical dosage formulations, or an oral dosage formulation of a compound of formula I in **combination** with a topical dosage formulation of, e.g., **minoxidil**, or a single oral dosage formulation of a compound of formula I and another 5.alpha.-reductase inhibitor, in **combination** with a topical dosage formulation of, e.g., **minoxidil**. See, e.g., U.S. Pat. Nos. 4,596,812, 4,139,619 and WO 92/02225, published Feb. 20, 1992, for dosages and formulations of calcium. . .

AN 2000:44109 USPATFULL

PI US 6048869 20000411

L12 . . . 13 88' 1 3 540* 42
Statistically slgn1f1cant t-,4
WO 94/17663 PCT/US94/01373
The data in the above table demonstrates the synergistic effects ot tne **block**:ing **testosterone** induced reIrmth. of the involuted rat ventral prostate.



chemically **minoxidil** is designated as 2,4-pyrimidineadiamine, 6-(1-piperidinyl)-,3-oxide. **Minoxidil** is the active ingredient in Rogaine@ which is sold as topical solution for stimulating hair growth by the Upjohn Company, Kalamazoo, Michigan. When **minoxidil** is utilized in **combination** with 5-oc-reductase inhibitors, as described herein, **minoxidil** is preferably administered analogously to its commercial form.

AN 1994017663
P

L12 . . . PCTFULL COPYRIGHT 2001 MicroPatent

DETD Another approach described in United States Patent No. 5,183,817 is to utilize retinoids or mixtures thereof in **combination** with **minoxidil** and/or **minoxidil**-type compounds in stimulating or increasing the rate at which hair grows on mammalian skin. Such treatment does not reduce hormone production. It may. . .

. . .

disadvantages associated with this method are itching upon topical application, poor absorption, inconvenience in application, and the necessity of mussing of the hair. Furthermore, **progesterone** and **progesterone**- like compounds are cited as preferred inhibitors in United States Patent No. 5,053,403. However, because **progesterone** and **progesterone**-like compounds do not completely inhibit the conversion of testosterone to dihydrotestosterone, such agents do not provide suitable hair growth.

treatment of male-pattern baldness is finasteride, a synthetic 4-azasteroid compound, sold under the name Proscarl '. Finasteride is structurally similar to **progesterone**. ProscarO has been used to shrink enlarged prostates by blocking the formation of DHT. However, ProscarO does not provide an efficacious treatment of. . .

LHRH antagonists, however, suppress **testosterone** formation by **blocking** LH release by competitive antagonism of LHRH binding at the pituitary receptor level. Accordingly, levels of dihydrotestosterone, the hormone principally responsible for causing male. . .

A

4/9,K/22 (Item 1 from file: 156)
DIALOG(R)File 156:Toxline(R)

02537123 Subfile: TOXBIB-92-113079

Hair growth effects of oral administration of finasteride, a steroid 5 alpha-reductase inhibitor, alone and in combination with topical minoxidil in the balding stumptail macaque.

Diani AR; Mulholland MJ; Shull KL; Kubicek MF; Johnson GA; Schostarez HJ; Brunden MN; Buhl AE

Upjohn Laboratories, Kalamazoo, Michigan 49001.

Source: J Clin Endocrinol Metab; VOL 74, ISS 2, 1992, P345-50 ISSN: 0021-972X Coden: HRB

Language: ENGLISH

Document Type: JOURNAL ARTICLE

Journal Announcement: 9204

A 5 alpha-reductase inhibitor, finasteride, was administered orally at 0.5 mg/day, alone or in combination with topical 2% minoxidil, for 20 weeks to determine the effects on scalp **hair** growth in balding adult male stumptail macaque monkeys. A 7-day dose-finding study showed that both 0.5- and 2.0-mg doses of the drug produced a similar diminution in serum dihydrotestosterone (DHT) in male stumptails. **Hair** growth was evaluated by shaving and weighing scalp **hair** at baseline and at 4-week intervals during treatment to obtain cumulative delta **hair** weight (sum of the 4-week changes in **hair** weight from baseline) for the 20-week study. The activity of the 5 alpha-reductase enzyme was assessed by RIA of serum testosterone (T) and DHT at 4-week intervals. The combination of finasteride and minoxidil generated significant augmentation of **hair** weight (additive effect) compared to either drug alone. Finasteride increased **hair** weight in four of five monkeys. When the data of the one nonresponsive monkey were excluded, finasteride elicited a significant elevation in **hair** weight compared to topical vehicle alone. Minoxidil also evoked a significant increase in **hair** weight compared to vehicle alone. Serum T was unchanged, whereas serum DHT was significantly depressed in monkeys that received either finasteride or the combination of finasteride and minoxidil. These data suggest that inhibition of the conversion of T to DHT by this 5 alpha-reductase inhibitor reverses the balding process and enhances **hair** regrowth by topical minoxidil in the male balding stumptail macaque.

Tags: Animal; Male

Descriptors/Keywords: Androstenes--Pharmacology--PD; *Azasteroids --Pharmacology--PD; *Hair--Drug Effects--DE; *Minoxidil--Pharmacology --PD; *Testosterone 5-alpha-Reductase--Antagonists and Inhibitors--AI; Administration, Oral; Administration, Topical; Androstenes--Administration and Dosage--AD; Azasteroids--Administration and Dosage--AD; Chromatography, High Pressure Liquid; Drug Interactions; Hair--Physiology--PH; Macaca ; Minoxidil--Administration and Dosage--AD; Minoxidil--Urine--UR; Reference Values; Stanolone--Blood--BL; Testosterone--Blood--BL

CAS Registry No.: 0 (Androstenes); 0 (Azasteroids); 38304-91-5 (Minoxidil); 521-18-6 (Stanolone); 57-85-2 (Testosterone); 98319-26-7 (Finasteride)

Enzyme No.: EC 1.3.99.5 (Testosterone 5-alpha-Reductase)

Hair growth effects of oral administration of finasteride, a steroid 5 alpha-reductase inhibitor, alone and...

Diani AR; Mulholland MJ; Shull KL; Kubicek MF; Johnson GA; Schostarez HJ; Brunden MN; Buhl AE

... in combination with topical 2% minoxidil, for 20 weeks to determine the effects on scalp **hair** growth in balding adult male stumptail

macaque monkeys. A 7-day dose-finding study showed...

... doses of the drug produced a similar diminution in serum dihydrotestosterone (DHT) in male stumptails. **Hair** growth was evaluated by shaving and weighing scalp **hair** at baseline and at 4-week intervals during treatment to obtain cumulative delta **hair** weight (sum of the 4-week changes in **hair** weight from baseline) for the 20-week study. The activity of the 5 alpha-reductase...

... DHT at 4-week intervals. The combination of finasteride and minoxidil generated significant augmentation of **hair** weight (additive effect) compared to either drug alone. Finasteride increased **hair** weight in four of five monkeys. When the data of the one nonresponsive monkey were excluded, finasteride elicited a significant elevation in **hair** weight compared to topical vehicle alone. Minoxidil also evoked a significant increase in **hair** weight compared to vehicle alone. Serum T was unchanged, whereas serum DHT was significantly depressed...
... T to DHT by this 5 alpha-reductase inhibitor reverses the balding process and enhances **hair** regrowth by topical minoxidil in the male balding stumptail macaque.

Descriptors/Keywords: Androstenes--Pharmacology--PD; *Azasteroids --Pharmacology--PD; ***Hair**--Drug Effects--DE; *Minoxidil--Pharmacology --PD; *Testosterone 5-alpha-Reductase--Antagonists and Inhibitors--AI...; Administration and Dosage--AD; Azasteroids--Administration and Dosage--AD; Chromatography, High Pressure Liquid; Drug Interactions; **Hair** --Physiology--PH; Macaca; Minoxidil--Administration and Dosage--AD; Minoxidil--Urine--UR; Reference Values; Stanolone--Blood...

8/3,K/16 (Item 1 from file: 453)
DIALOG(R)File 453:Drugs of the Future

00145770 (Structure Image Available)
ENTRY NUMBER: 145770
DRUG NAME: MK-906
YM-152
GENERIC NAME Finasteride (recommended INN; BAN; USAN)
BRAND NAME: Andozac
Chibro-Proscar (Merck Sharp & Dohme, FR)
Finastid
Prodel (Yamanouchi, JP)
Propecia (Merck & Co., US;Merck Sharp & Dohme, ES, FR, IT)
Proscar (Banyu, JP;Merck Sharp & Dohme, ES, GB, IT, SE, US)
Prostide (Sigma-Tau, IT)
CHEM NAME: 17beta-(N-tert-Butylcarbamoyl)-4-aza-5alpha-androst-1-en-3-one
N-tert-Butyl-3-oxo-4-aza-5alpha-androst-1-ene-17beta-carboxamide
FORMULA: C23H36N2O2
CAS REG. NO.: 98319-26-7
DEVEL. PHASE: Launched (201992)
ORIGINATOR: Banyu
DuPont Pharmaceuticals
Merck & Co.
Merck Sharp & Dohme
LICENSEE: Sigma-Tau
Yamanouchi
CLASS: 35560 (Benign Prostatic Hyperplasia Therapy)
41515 (Hirsutism Therapy)
59813 (Hair Growth Stimulants)
40120 (Antiandrogens)
78335 (Steroid 5alpha-Reductase Inhibitors)
SYNTHESIS: 20604
68332
65430
CONTEXT TABLE: 35560C (Benign Prostatic Hyperplasia Therapy)

...p.o. finasteride was found to reverse balding and enhance hair regrowth alone and in **combination** with topical **minoxidil** via inhibition of conversion of **testosterone** to dihydrotestosterone. (60)

In healthy volunteers administered oral (14C)-finasteride (38.1 mg), mean peak...

8/3,K/14 (Item 1 from file: 377)
DIALOG(R)File 377:Derwent Drug File

00538206 DERWENT ACCESSION NUMBER: 93-27559
Isotretinoin Reduces Amount of **Dihydrotestosterone** Produced in Scalp Skin and Promotes Hair Growth in **Combination** With **Minoxidil**.
Bazzano G S; Terezakis N K
J.Invest.Dermatol. 100, No. 4, 545, 1993

Isotretinoin Reduces Amount of **Dihydrotestosterone** Produced in Scalp Skin and Promotes Hair Growth in **Combination** With **Minoxidil**.

ABSTRACT:
...could reduce the size of scalp sebaceous glands and thereby reduce their capacity to produce **dihydrotestosterone** (DHT, androstanolone), 8 patients were evaluated following isotretinoin treatment. Scalp sebum secretion was reduced and tritiated **testosterone** conversion to DHT in whole scalp biopsies was reduced. In another group of 10 patients isotretinoin in **combination** with **minoxidil** promoted hair growth. The results suggest that topical 13-cis retinoic acid (isotretinoin) can suppress DHT production and in **combination** with **minoxidil**, stimulates hair growth in a synergistic manner. (congress

16/3,K/11 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03081929 Genuine Article#: NC132 No. References: 31
Title: ENDOCRINE PROPERTIES OF THE TESTOSTERONE 5-ALPHA-REDUCTASE INHIBITOR TUROSTERIDE (FCE-26073)
Author(s): DISALLE E; BRIATICO G; GIUDICI D; ORNATI G; PANZERI A
Corporate Source: FARMITALIA CARLO ERBA SPA,R&D,ENDOCRINOL LAB,VIA GIOVANNI XXIII/I-20014 NERVIANO//ITALY/
Journal: JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, 1994, V48, N2-3 (FEB), P241-248
ISSN: 0960-0760
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

...Abstract: androgens (relative binding affinity, RBA, 0.004%), estrogens (less-than-or-equal-to 0.005%), **progesterone** (<0.005%), glucocorticoids (<0.01%) and mineralocorticoids (<0.03%). Its biochemical profile was similar to that of **finasteride**, whereas 4-MA (17beta-N,N-diethyl-carbamoyl-4-methyl-4-aza-5alpha-androstan-3...
...Identifiers--HUMAN STEROID 5-ALPHA-REDUCTASE; BENIGN PROSTATIC HYPERPLASIA; RAT; **FINASTERIDE**; DEHYDROGENASE; AROMATASE; ISOMERASE

16/3,K/10 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04683633 Genuine Article#: UA127 No. References: 35
Title: EFFECT OF **PROGESTERONE**, TESTOSTERONE AND THEIR 5-ALPHA-REDUCED METABOLITES ON GFAP GENE-EXPRESSION IN TYPE-1 ASTROCYTES
Author(s): MELCANGI RC; RIVA MA; FUMAGALLI F; MAGNAGHI V; RACAGNI G; MARTINI L
Corporate Source: UNIV MILAN,INST PHARMACOL SCI,DEPT ENDOCRINOL,VIA G BALZARETTI 9/I-20133 MILAN//ITALY/; UNIV MILAN,INST PHARMACOL SCI,CTR NEUROPHARMACOL/I-20133 MILAN//ITALY/; HOSP SAN RAFFAELE,DIBIT/I-20132 MILAN//ITALY/
Journal: BRAIN RESEARCH, 1996, V711, N1-2 (MAR 4), P10-15
ISSN: 0006-8993
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

Title: EFFECT OF **PROGESTERONE**, TESTOSTERONE AND THEIR 5-ALPHA-REDUCED METABOLITES ON GFAP GENE-EXPRESSION IN TYPE-1 ASTROCYTES
...Abstract: typical of steroid target cells, such as 5 alpha-reductase, which converts testosterone (T) and **progesterone** (P) into their respective 5 alpha-reduced metabolites, and the 3 alpha-hydroxysteroid dehydrogenase (3...

...its conversion into DHP; this hypothesis has been confirmed by showing that the addition of **finasteride** (a specific blocker of the 5 alpha-reductase) is able to completely abolish the effect...

16/3,K/7 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07329820 Genuine Article#: 151GB No. References: 43
Title: An ongoing validation of a Tier I screening battery for detecting endocrine-active compounds (EACs)
Author(s): OConnor JC; Cook JC (REPRINT) ; Slone TW; Makovec GT; Frame SR; Davis LG
Corporate Source: DUPONT CO INC,HASKELL LAB TOXICOL & IND MED, POB 50/NEWARK//DE/19714 (REPRINT); DUPONT CO INC,HASKELL LAB TOXICOL & IND MED/NEWARK//DE/19714
Journal: TOXICOLOGICAL SCIENCES, 1998, V46, N1 (NOV), P45-60
ISSN: 1096-6080 Publication date: 19981100
Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495
Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

...Abstract: receptor antagonist (flutamide, FLUT), a testosterone biosynthesis inhibitor (ketoconazole, KETO), a 5 alpha-reductase inhibitor (**finasteride**, FIN), and an aromatase inhibitor (anastrozole, ANA). The Tier I battery incorporates two short-term...

...compounds that have the potential to act as agonists or antagonists to the estrogen, androgen, **progesterone**, or dopamine receptors, steroid biosynthesis inhibitors (aromatase, 5 alpha-reductase, and testosterone biosynthesis), or compounds that alter thyroid function. ICI administration decreased uterine estrogen and **progesterone** receptor number in the female battery, increased serum follicle-stimulating hormone (FSH) levels and caused...
...Identifiers--TESTICULAR TOXICITY; ANDROGEN RECEPTOR; BORIC-ACID; RAT; TRANSCRIPTION; **5-ALPHA-REDUCTASE**; KETOCONAZOLE; ANTIANDROGEN; DERIVATIVES; **FINASTERIDE**

16/3,K/8 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05435885 Genuine Article#: VY583 No. References: 51
Title: SCREENING FOR DRUG-INDUCED ALTERATIONS IN THE PRODUCTION AND RELEASE OF STEROID-HORMONES BY PORCINE ADRENOCORTICAL-CELLS IN-VITRO
Author(s): JAGER LP; DEGRAAF GJ; WIDJAJAGREEFKES HCA
Corporate Source: DLO,CENT VET INST,DEPT BIOCHEM & TOXICOL,POSTBUS 65/NL-8200 AB LELYSTAD//NETHERLANDS/
Journal: TOXICOLOGY IN VITRO, 1996, V10, N5 (OCT), P595-608
ISSN: 0887-2333
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

...Abstract: potential to alter steroidogenesis, an in vitro model using porcine adrenocortical cells was developed. Pregnenolone, **progesterone**, deoxycorticosterone or corticosterone (all at 1 mu M) were used as substrates. Drug-induced changes...

...pregnenolone, drug-induced effects on the release of nine steroids (aldosterone, corticosterone, cortisol, deoxycortisol, testosterone, **progesterone**, HO-**progesterone**, androstenedione, dehydroepiandrosterone) were monitored simultaneously. For assessment

of cell viability and the amount of steroids...
...Aminoglutethimide inhibited the release of aldosterone with corticosterone as substrate, but not with deoxycorticosterone or **progesterone** as substrate, revealing an alternative pathway in the biogenesis of aldosterone by-passing corticosterone. Trilostane (0.1-1 mu M) completely blocked conversion of pregnenolone to **progesterone** and OH-**progesterone**; the release of androstenedione was at most only halved, whereas the release of dehydroepiandrosterone and...

...enzymes involved in transformations at C21 and at C17, respectively. Cyproheptadine blocks all transformations with **progesterone** or HO-**progesterone** as starting point. **Finasteride** reduced the release of most steroids, except the androgens, presumably by inhibition of transformations at...
...Identifiers--ALDOSTERONE BIOSYNTHESIS; ADRENAL STEROIDOGENESIS; IMIDAZOLE DERIVATIVES; DOSE KETOCONAZOLE; WEANED PIGS; IN-VITRO; ETOMIDATE; INHIBITION; CORTISOL; **5-ALPHA-REDUCTASE**